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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,575	09/30/2003	Sudhir K. Sinha	P56885	2640

7590 10/02/2007

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EXAMINER	
BABIC, CHRISTOPHER M	
ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
10/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/673,575	SINHA ET AL.	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-9 and 21-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5, 7-9, 21-24* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claim(s) 1, 5-9, and 21-24 are pending. The following Office Action is in response to Applicant's response dated July 17, 2007.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claim(s) 1, 7, 8, and 21-24 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis et al. ("A more sensitive method for the quantitation of genomic DNA by Alu amplification" J Forensic Sci. 2002 May;47(3):589-92) in view of Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434), in further view of Jurka ("A new subfamily of recently retroposed human Alu repeats" Nucleic Acids Research. 1993. Vol. 21. No. 9, Page 2252) as evidenced by Batzer et al. ("Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, pg. 3-6).

With regard to claim(s) 1, 21, and 22, Sifis teaches a method (pg. 589, 590, materials and methods, for example) comprising: providing a sample to be analyzed (pg. 589, 590, materials and methods, amplification, for example); amplifying predetermined genomic DNA containing an Alu element by using primers (pg. 589, 590, materials and methods, amplification, for example), the amplification being intra-Alu polymerase chain reaction amplification (pg. 589, 590, materials and methods, amplification, for example); and measuring the amount the human DNA by comparing the amplified DNA with a reference (fig. 1, 2; pg. 589, 590, materials and methods, amplification, for example).

With regard to claim 8, Sifis teaches detecting the human DNA using a quantitative PCR system (pg. 590, col. 1, for example).

Sifis further teaches that the assay is based on the amplification of core Alu sequences, i.e. intra-Alu PCR, from primate DNA (pg. 589, 590, materials and methods, amplification, for example). Sifis further highlights that it is desirable that any method of quantitation be **primate specific**; otherwise, any substantial contamination may lead to overestimation of the amount of primate DNA within the sample DNA extract. Sifis does not however, expressly teach the amplification of Alu sequences that are contained exclusively in the human genome.

Palmirotta provides a supporting disclosure that teaches the PCR amplification of Alu sequences for the specific purpose of determining the origin of the DNA (i.e. human DNA or non-human primate DNA) (pg. 432, col. 1, PCR amplification, for example). Palmirotta expressly teaches that PCR-based methods **targeting human Alu** sequences may contribute to the evaluation of biological samples of suspected human origin (pg. 431, col. 2, para. 4, for example). Thus, it is clear from the teachings of Palmirotta that the amplification of Alu sequences that are not exclusively contained within the human genome, from an unknown nucleic acid sample, can lead to amplification of unwanted primate DNA, e.g. non-human primates DNA.

With regard to claim 7, Palmirotta teaches detecting the human DNA on an agarose gel stained with ethidium bromide (Figure 1).

Thus, Palmirotta does not teach the amplification of Alu sequences that are contained exclusively in the human genome.

Jurka provides a supporting disclosure that teaches the discovery of an Alu, mutation specific, subfamily Sb2 (see reference: Batzer et al. "Standardized

Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, fig. 1, pg. 3-6, for example) **exclusively contained** within the human genome that is particularly suited for experimental probing (pg. 2252, col. 1, for example). Thus, it is clear from the teachings of Jurka that Alu sequences exclusively contained within the human genome were well known in the art at the time of invention.

Thus, it is asserted that a practitioner of ordinary skill in the art at the time of invention wanting to quantify human DNA from an **unknown source** through the method of Sifis would have been motivated select an Alu known to reside strictly within the human genome to obtain accurate human results. Thus, it would have been *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention to practice the methods as claimed.

With regard to claim(s) 23 and 24, given that it is clear from the teachings of Jurka that Alu sequences exclusively contained within the human genome were well known in the art at the time of invention, it would have been further *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention to incorporate primers that are complementary to the specific Alu sequence.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. Applicant first argues that the prior art does not suuggest the desirability of the claimed invention. Applicant asserts that if, as stated by the Examiner, there is no benefit from the amplification of an Alu sequence there is no desirability of combination or

modification. This argument is not persuasive because the Examiner is not asserting that there is no benefit from the amplification of an Alu sequence. Instead, the Examiner is asserting that the methods taught by Sifis and Palmirotta did not necessarily require or even benefit from the amplification of an Alu sequence **exclusively contained within the human genome**. As presented previously, the methods of Palmirotta teach methods of determining the origin of a sample of DNA of unknown origin. Not knowing if the sample was from a non-human primate (e.g. gorilla, chimpanzee, etc.), it would not have been necessarily beneficial to assay an Alu sequence exclusively contained within the human genome. Second, the items swabbed and analyzed within table 3 of Sifis, show samples (e.g. glove, cup, elevator button) that would have very little chance if any of containing non-human primate (e.g. gorilla, chimpanzee, etc.) DNA, i.e. there is very little chance of contaminating non-primate DNA on an elevator button. Thus, it would not have been necessary to assay an Alu sequence exclusively contained within the human genome because there was virtually no chance of inaccurate results due to contaminating non-primate DNA. However, a practitioner of ordinary skill in the art at the time of invention wanting to quantify **strictly** human DNA from an unknown source (e.g. a crime scene) through the method of Sifis would have been motivated select an Alu known to reside strictly within the human genome to obtain accurate human results.

Applicant next argues that "a general incentive" or an "obvious to try situation" does not make the invention obvious. This argument is not persuasive because first, the Examiner provides a clear motivation to select an Alu sequence contained

exclusively within the human genome, i.e. wanting to quantify **strictly** human DNA from an unknown source (e.g. a crime scene) through the method of Sifis would have been motivated select an Alu known to reside strictly within the human genome to obtain accurate human results. Furthermore, in the recent court decision, *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007), the court held that, " When there is a design need or market pressure to solve a problem and there are a finite number of identified, **predictable solutions**, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the **anticipated success**, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was **obvious to try** might show that it was obvious under §103."

Applicant further argues, as understood by the Examiner, that the prior art is not enabled, because Jurka in combination with Sifts et al. and Palmirotta et al. does teach how to make the primers from Sb2 for the PCR protocol from which the mount of the human DNA can be quantitated as described in Sifis et al. This argument is not persuasive because designing primers to a known sequence was well within the capability of a skilled artisan at the time of invention. If Applicant is attempting to argue that the primers used by Applicant provide unexpected results, Applicant is first reminded that claim 6 is has been found to be free of the prior art, and furthermore, Applicant is invited to provide evidence of such results. Furthermore, with regard to claim(s) 23 and 24, given that it is clear from the teachings of Jurka that Alu sequences exclusively contained within the human genome were well known in the art at the time

of invention, it would have been further *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention to incorporate primers that are complementary to the specific Alu sequence.

Thus, the rejections are maintained.

2. Claims 5 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis et al. ("A more sensitive method for the quantitation of genomic DNA by Alu amplification" J Forensic Sci. 2002 May;47(3):589-92) in view of Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434), in further view of Jurka ("A new subfamily of recently retroposed human Alu repeats" Nucleic Acids Research. 1993. Vol. 21. No. 9, Page 2252) as evidenced by Batzer et al. ("Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, pg. 3-6) as applied to claim(s) 1, 7, 8, 21, and 22 above, and in further view of Buck et al. ("Design Strategies and Performance of Custom DNA Sequencing Primers") BioTechniques. September 1999. 27: Pages 528-536).

Regarding claim(s) 5, the methods of the previously applied references have been outlined in the above rejections. The previously applied references do not expressly disclose the *exact* primer sequences of SEQ ID NO: 3 and SEQ ID NO: 4, drawn to the "young" Yb8 Alu subfamily.

Jurka discloses the entire Sb2 Alu subfamily sequence (fig. 1, for example). The term "Sb2" is considered to be older nomenclature of the "young" Yb8 subfamily (see reference: Batzer et al. "Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, pg. 3-6, for example).

The *identical* sequence presented in SEQ ID NO: 3 (5'-CGAGGCGGGTGGATCATGAGGT-3' is contained in the sequence provided by Jurka (fig. 1, for example) from nucleotides 48-69. Furthermore, the *identical* complement of the sequence (i.e. reverse primer) presented in SEQ ID NO: 4 (5'-TCTGTCGCCCAGGCCGGACT -3' is contained in the sequence provided by Jurka (fig. 1, for example) from nucleotides 273-254.

Buck provides a supporting disclosure that expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (pg. 532, col. 3, for example), with 69 different primers being submitted (pg. 530, col. 1, for example). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (pg. 530, col. 1, for example). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (pg. 533, col. 1, for example). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (pg. 533, col. 1, for example). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (pg. 535, col. 2, for example)."

Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Thus, since the claimed primers simply represent complementary functional homologs of the sequences taught by Jurka, the claimed primers are *prima facie* obvious over Jurka in view Buck et al.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive.

Applicant argues that the "structural similarity" doctrine does not apply in this case. This argument is not persuasive because the DNA in this case is not mediating cell phisiology. In this case, the DNA oligomers are being used strictly to amplify DNA.

Applicant further argues that a prior art disclosing the sequence of a certain gene does not automatically make the particular DNA primers amplifying the specific region of the certain gene obvious. This argument is not persuasive because the rejection of claim 5 is based upon Jurka in combination with Buck, who expressly demonstrates the equivalence of primers. Applicant further asserts that a vast number of target sequences are possible from the known DNA sequence, and the reference did not teach or fairly suggest the selection of the sequences of claim 5. This argument is not persuasive because the number of possibilities does not detract from the fact that a

skilled artisan would have expected primers drawn to sections of known sequences to be able to function as primers.

Applicant finally argues that Buck does not discuss primers in the PCR context, but only in the sequencing context. This is not persuasive because in both contexts, the primers function in a similar manner. In both cases, the primers must hybridize to the appropriate site on the target and be capable of extension. Nothing more or less is required of the primer in one situation over the other. Again, if Applicant is attempting to argue that the primers used by Applicant provide unexpected results, Applicant is first reminded that claim 6 is has been found to be free of the prior art, and furthermore, Applicant is invited to provide evidence of such results.

Thus, the rejection is maintained.

3. Claim(s) 9 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis et al. ("A more sensitive method for the quantitation of genomic DNA by Alu amplification" J Forensic Sci. 2002 May;47(3):589-92) in view of Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434), in further view of Jurka ("A new subfamily of recently retroposed human Alu repeats" Nucleic Acids Research. 1993. Vol. 21. No. 9, Page 2252) as evidenced by Batzer et al. ("Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, pg. 3-6) as applied to claim(s) 1, 7, 8, 21, and 22 above, and in further view of Gelmini et al. ("Quantitative polymerase chain

reaction-based homogeneous assay with fluorogenic probes to measure c-*erb*B-2 oncogene amplification" Clinical Chemistry. 1997. 43:5, Pages 752-758).

Regarding claim(s) 9, the methods of the previously applied references have been outlined in the above rejections. The previously applied references do not specifically disclose the practice of a quantitative PCR system such as *Taq*Man.

Gelmini provides a supporting disclosure that teaches the practice of a quantitative PCR system using *Taq*Man chemistry (fig. 1,2,3; table 1; pg. 754, Columns 1,2, for example). Furthermore, they highlight the advantages of using fluorogenic probes in PCR, such as the circumventing of post-PCR product quantitation procedures (pg. 752, col. 2, para. 2, for example).

It would have been *prima facie* obvious to a practitioner ordinary skill in the art at the time of invention to incorporate a quantitative PCR system into the methods of Sifis since Gelmini suggests such a modification for among other reasons, to circumvent post-PCR product quantitation procedures.

Allowable Subject Matter

As noted previously, claim(s) 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

None of the previously applied references teach or suggest the amplification of the AluYd6 subfamily of human specific Alu elements. The sequences presented in SEQ ID NOs: 5 and 6 are novel and unobvious over the prior art.

Conclusion

Claim(s) 1, 5, 7-9, and 21-24 are rejected.

Claim(s) 6 is objected to.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-

272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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9/27/07